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Commissioner for Patents
Washington, D.C. 20231

Re: U.S. Patent Application No.: 09/914451
For: *DRUG DESIGN BASED ON THE STRUCTURE OF LTA$_4$ HYDROLASE*
Inventors: Jesper Z. Haeggström *et al.*
Filed: August 27, 2001
Our Ref. No.: PVZ-006US

Dear Sir:

I enclose herewith for filing in the above-identified application the following:

1. Information Disclosure Statement;
2. PTO Form 1449;
3. Copies of references cited in PTO Form 1449 (43); and
4. A Return Postcard.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080. For this purpose, a duplicate of this sheet is attached.

I hereby certify that this correspondence is deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231 on:

12/19/02
Date

Elizabeth A. Hanley, Reg. No. 33,505

Respectfully submitted,
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Elizabeth A. Hanley
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Jesper Z. Haeggström *et al.*

Serial No.: 09/914451

Filed: August 27, 2001

For: *DRUG DESIGN BASED ON THE STRUCTURE OF LTA4 HYDROLASE*

Attorney Docket No.: PVZ-006US

Group Art Unit: 1642

Examiner: Not yet assigned

Commissioner for Patents
Washington, D.C. 20231

Certificate of First Class Mailing (37 CFR §1.8(a))

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Date of Signature and of Mail Deposit

By: EAHanley
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INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Applicants and their Attorney are aware of the following publications and information, listed on the attached PTO Form 1449, and in accordance with 37 CFR §1.97 hereby submit these publications for the Examiner's consideration. A copy of each cited publication is enclosed.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other

relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited publications.

Under 37 C.F.R. § 1.97(b)(3), no additional costs are believed to be due in connection with the filing of this disclosure. If, however, a first Office Action on the merits issues in this application bearing a mailing date prior to the date of this Information Disclosure Statement, please charge the appropriate fee as required under 37 CFR §1.17(p) to our Deposit Order Account No. 12-0080.

Respectfully submitted,
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Enclosures

APPLICANT FACSIMILE OF FORM PTO-1449 REV. 9-80	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY DOCKET NO	SERIAL NO.
LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		PVZ-006US	09/914457
		APPLICANT: Jesper Z. Haeggstr¨m et al.	
		FILING DATE: August 27, 2001	GROUP: 1642

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

	A1		Andberg, M. et al. "Mutation of tyrosine 383 in leukotriene A_4 hydrolase allows conversion of leukotriene A_4 into 5S,6S-dihydroxy-7,9-trans-11,14-cis-eicosatetraenoic acid. Implications for the epoxide hydrolase mechanism," *J. Biol. Chem.* 1997 Sep 12;272(37):23057-63
	A2		Barrett, A.J. et al. Eds. "336. Introduction: family M1 of membrane alanyl aminopeptidase," in Handbook of proteolytic enzymes 1998 Oct; pp. 994-996
	A3		Blomster, M. et al. "Evidence for a catalytic role of tyrosine 383 in the peptidase reaction of leukotriene A_4 hydrolase," *Eur. J. Biochem.* 1995 Aug 1;231(3):528-34
	A4		Byrum, R.S. et al. "Determination of the contribution of cysteinyl leukotrienes and leukotriene B_4 in acute inflammatory responses using 5-lipoxygenase- and leukotriene A_4 hydrolase-deficient mice," *J. Immunol.* 1999 Dec 15;163(12):6810-9
	A5		Chen, X.-S. et al. "Role of leukotrienes revealed by targeted disruption of the 5-lipoxygenase gene," *Nature* 1994 Nov;372:179-182
	A6		Crameri, A. et al. "DNA shuffling of a family of genes from diverse species accelerates directed evolution," *Nature* 1998 Jan 15;391(6664):288-91
	A7		Devchand, P.R. et al. "The PPARalpha-leukotriene B_4 pathway to inflammation control," *Nature* 1996 Nov 7;384(6604):39-43
	A8		Dittmann, K.H. et al. "MK-886, a leukotriene biosynthesis inhibitor, induces antiproliferative effects and apoptosis in HL-60 cells," *Leuk. Res.* 1998 Jan;22(1):49-53
	A9		Drazen, J.M. et al. "Treatment of asthma with drugs modifying the leukotriene pathway," *N. Engl. J. Med.* 1999 Jan 21;340(3):197-206
	A10		Evans, J.F. "Leukotriene A_3. A poor substrate but a potent inhibitor of rat and human neutrophil leukotriene A_4 hydrolase," *J. Biol. Chem.* 1985 Sep 15;260(20):10966-70
	A11		Ford-Hutchinson, A.W. et al. "Leukotriene B, a potent chemokinetic and aggregating substance released from polymorphonuclear leukocytes," *Nature* 1980 July 17;286:264-65
	A12		Funk, C.D. et al. "Molecular cloning and amino acid sequence of leukotriene A_4 hydrolase," *Proc. Natl. Acad. Sci. USA* 1987 Oct;84(19):6677-81
	A13		Griffiths, R.J. et al. "Leukotriene B_4 plays a critical role in the progression of collagen-induced arthritis," *Proc. Natl. Acad. Sci. USA* 1995 Jan 17;92(2):517-21
	A14		Griffiths, R.J. et al. "Collagen-induced arthritis is reduced in 5-lipoxygenase-activating protein-deficient mice," *J. Exp. Med.* 1997 Mar 17;185(6):1123-9

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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		PVZ-006US	09/91445
		APPLICANT: Jesper Z. Haeggström t al.	
		FILING DATE: August 27, 2001	GROUP: 1642

U.S. PATENT DOCUMENTS

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FOREIGN PATENT DOCUMENTS

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OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

	B1		Haeggström, J.Z. et al. "Leukotriene A_4 hydrolase: structural and functional properties of the active center," *J. Lipid Mediat.* 1993 Mar-Apr;6(1-3):1-13
	B2		Hogg, J.H. et al. "Probing the activities and mechanisms of leukotriene A_4 hydrolase with synthetic inhibitors," *Chem. Eur. J.* 1998;4(9):1698-1713
	B3		Kuchner, O. et al. "Directed evolution of enzyme catalysts," *Trends Biotechnol.* 1997 Dec;15(12):523-30
	B4		Labaudinière, R. et al. "ω -[(ω-Arylalkyl)thienyl]alkanoic acids: from specific LTA_4 hydrolase inhibitors to LTB_4 receptor antagonists," *J. Med. Chem.* 1992 Aug 21;35(17):3170-9
	B5		Lewis, R.A. et al. "Leukotrienes and other products of the 5-lipoxygenase pathway. Biochemistry and relation to pathobiology in human diseases," *N. Engl. J. Med.* 1990 Sep 6;323(10):645-55
	B6		Lorsch, J.R. et al. "In vitro evolution of new ribozymes with polynucleotide kinase activity," *Nature* 1994 Sep 1;371(6492):31-6
	B7		Medina, J.F. et al. "Leukotriene A_4 hydrolase: determination of the three zinc-binding ligands by site-directed mutagenesis and zinc analysis," *Proc. Natl. Acad. Sci. USA* 1991 Sep 1;88(17):7620-4
	B8		Ménard, A. et al. "The cytotoxic activity of Bacillus anthracis lethal factor is inhibited by leukotriene A_4 hydrolase and metallopeptidase inhibitors," *Biochem. J.* 1996 Dec 1;320 (Pt 2):687-91
	B9		Mueller, M.J. et al. "Leukotriene A_4 hydrolase: mapping of a henicosapeptide involved in mechanism-based inactivation," *Proc. Natl. Acad. Sci. USA* 1995 Aug 29;92(18):8383-7
	B10		Mueller, M.J. et al. "Leukotriene A_4 hydrolase: protection from mechanism-based inactivation by mutation of tyrosine-378," *Proc. Natl. Acad. Sci. USA* 1996 Jun 11;93(12):5931-5
	B11		Mueller, M.J. et al. "Leukotriene A_4 hydrolase, mutation of tyrosine 378 allows conversion of leukotriene A_4 into an isomer of leukotriene B_4," *J. Biol. Chem.* 1996 Oct 4;271(40):24345-8
	B12		Nord, K. et al. "Binding proteins selected from combinatorial libraries of an alpha-helical bacterial receptor domain," *Nat. Biotechnol.* 1997 Aug;15(8):772-7
	B13		Orning, L. et al. "Inhibition of leukotriene A_4 hydrolase/aminopeptidase by captopril," *J. Biol. Chem.* 1991 Sep 5;266(25):16507-11
	B14		Orning, L. et al. "The bifunctional enzyme leukotriene- A_4 hydrolase is an arginine aminopeptidase of high efficiency and specificity," *J. Biol. Chem.* 1994 Apr 15;269(15):11269-73

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APPLICANT FACSIMILE OF FORM PTO-1449 REV 7-80	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY DOCKET NO	SERIAL NO.
LIST OF PUBLICATIONS CITED BY APPLICANT (Use several sheets if necessary)		PVZ-006US	09/914451
		APPLICANT Jesper Z. Haeggström et al.	RECEIVED
		FILING DATE August 27, 2001	GROUP 1642 DEC 27 2002

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U.S. PATENT DOCUMENTS

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FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

	C1		Owman, C. et al. "The leukotriene B_4 receptor functions as a novel type of coreceptor mediating entry of primary HIV-1 isolates into CD4-positive cells," *PNAS. USA* 1998 Aug 4;95(16):9530-4
	C2		Rola-Pleszczynski, M. et al. "Leukotrienes augment interleukin 1 production by human monocytes," *J. Immunol.* 1985 Dec;135(6):3958-61
	C3		Samuelsson, B. "Leukotrienes: mediators of immediate hypersensitivity reactions and inflammation," *Science* 1983 May 6;220(4597):568-75
	C4		Samuelsson, B. et al. "Leukotrienes and lipoxins: structures, biosynthesis, and biological effects," *Science* 1987 Sep 4;237(4819):1171-6
	C5		Serhan, C.H. et al. "Lipid mediator networks in cell signaling: update and impact of cytokines," *FASEB J.* 1996 Aug;10:1-12
	C6		Tsuge, H. et al. "Crystallization and preliminary X-ray crystallographic studies of recombinant human leukotriene A_4 hydrolase complexed with bestatin," *J. Mol. Biol.* 1994 May 20;238(5):854-6
	C7		Vallee, B.L. et al. "Active-site zinc ligands and activated H_2O of zinc enzymes," *Proc. Natl. Acad. Sci. USA* 1990 Jan;87(1):220-4
	C8		Wetterholm, A. et al. "Recombinant mouse leukotriene A_4 hydrolase: a zinc metalloenzyme with dual enzymatic activities," *Biochim. Biophys. Acta* 1991 Oct 25;1080(2):96-102
	C9		Wetterholm, A. et al. "Leukotriene A_4 hydrolase: abrogation of the peptidase activity by mutation of glutamic acid-296," *Proc. Natl. Acad. Sci. USA* 1992 Oct 1;89(19):9141-5
	C10		Wetterholm, A. et al. "Potent and selective inhibitors of leukotriene A_4 hydrolase: effects on purified enzyme and human polymorphonuclear leukocytes," *J. Pharmacol. Exp. Ther.* 1995 Oct;275(1):31-7
	C11		Yamaoka, K.A. et al. "Leukotriene B_4 enhances activation, proliferation, and differentiation of human B lymphocytes," *J. Immunol.* 1989 Sep 15;143(6):1996-2000
	C12		Yokomizo, T. et al. "A G-protein-coupled receptor for leukotriene B_4 that mediates chemotaxis," *Nature* 1997 Jun 5;387(6633):620-4
	C13		Yokomizo, T. et al. "A second leukotriene B_4 receptor, BLT2. A new therapeutic target in inflammation and immunological disorders," *J. Exp. Med.* 2000 Aug 7;192(3):421-32
	C14		Yuan, W. et al. "Novel tight-binding inhibitors of leukotriene A_4 hydrolase," *J. Am. Chem. Soc.* 1992 April;114:6552-53
	C15		GenPept Acc. No. S65947; leukotriene-A4 hydrolase (EC 3.3.2.6) long isoform - human

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